strain or previous occupation with the pain. It is natural for a patient to think of strain where pain occurs in a joint or muscle, but it is never natural for him to think of strain when he has a pain in his belly. In every case the physician himself must seek to establish this connection by direct questioning.

The author wishes to express his grateful thanks to Dr. A. D. Irvine, of Edmonton, for his interest, co-operation and reports on the x-ray films.

OIL OF WINTERGREEN POISONING*

(REPORT OF TWO ADDITIONAL FATAL CASES)

BY W. T. SHIRREFF, M.D. AND L. N. PEARLMAN, M.D.

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ACCIDENTAL poisoning under any circumstances is an unfortunate event. However, when such an occurrence follows the ingestion of poisonous material which is readily available to the public without being designated a dangerous substance the event becomes tragic. Methyl salicylate (oil of wintergreen) is a drug which falls into the latter category. It may be purchased at any drug store without signature and without precautionary labels of either "poison" or "for external use only". It is, further, a substance used frequently as a household liniment and not uncommonly as a flavouring medium in foods.

With the general impression being that the drug is innocuous, it is not surprising to find that parents have permitted a child to play with a bottle of the oil. They are dumbfounded to learn that the child, should he swallow it in the course of a typical childish investigation of the substance, has indeed swallowed a substance which is as likely as not to produce a fatal result.

The following cases of methyl salicylate poisoning are being reported to bring again to the fore the potentially fatal properties of the drug.

CASE 1

A female child aged 15 months was admitted March 3, 1940, at 7 p.m. She had been transferred to the Strathcona Hospital for Contagious Diseases from the out-patient department of a local general hospital with a provisional diagnosis of laryngeal diphtheria.

A complete history was not available on admission although there was an accompanying note to the effect that on March 2, 1940, the infant had upset a bottle of oil of wintergreen and spilled some on its face.

Examination showed a moderately ill baby. Some hoarseness of the voice was present. Respirations were rapid (40). The temperature was 99.4° and the pulse was 140. The mouth and throat were red. No pharyngeal or nasal membrane was seen. Retraction of the chest was absent. The infant in other respects seemed normal. No evidence of dehydration was observed. A provisional diagnosis of hyperpnœa due to methyl salicylate ingestion was made. However, since no accurate history was available at the time, and since some hoarseness was present, 20,000 units of diphtheria antitoxin with epinephrine were given intramuscularly as a precautionary measure.

A catheter specimen of urine one hour later showed an acid reaction, no albumin, positive acetone, a very strongly positive ferric chloride reaction for salicylates and a faint reduction of Benedict's solution.

Shortly after this confirmation of the diagnosis, conversation with the mother revealed that the child had been a little hoarse on March 1st. On the morning of March 2nd, she played with a bottle of oil of wintergreen and apparently spilled some on her face. The amount originally in the bottle and the amount spilled were not known. One hour after the spilling, she vomited milk. Thereafter vomiting was "very frequent." About 6 hours after the ingestion of the poison the baby developed rapid breathing.

The parents had no idea that the bottle in reality contained a poison and did not call a physician until the morning of March 3rd. He advised immediate hospitalization. Late that afternoon the parents, still unaware of the seriousness of the situation, wandered down to a general hospital. The baby was seen by a member of the house staff. Apparently on account of the difficulty in breathing, the hoarseness and what was interpreted as being chest retraction, the baby was referred to us as a possible diphtheria case.

Once the diagnosis of diphtheria was discarded, the baby was put on hypotonic saline solutions with 5 per cent carbohydrate by mouth. A high colonic irrigation was given. Frequent alcohol sponging for small rises in temperature and a minimum of clothing were ordered. Morphine was given for restlessness. Following its administration, the baby rested much better and the breathing according to the nurses' notes was "less difficult". The respirations dropped to 22. Due to the diligence of the nursing staff 2,220 c.c. of fluid were given to the infant in her twenty-hours' stay at Strathcona. Fortunately, very little vomiting occurred (about 200 c.c.). It was noticed that the child's thirst was voracious. Voiding was very frequent and copious so that although urinary output was not measured there was a very good excretion.

Fourteen hours after admission the child was again seen by one of us. At that time the general condition was improved. Respirations were thirty per minute and pulse 116. During the interval, the temperature had risen to a maximum of 101° but had been reduced coincident with alcohol sponging. The CO_2 combining power of the blood was 35.7 volumes per cent at this time. The urine still showed acetone, salicylate, and reduction of Benedict's solution.

Nineteen hours after admission a specimen of urine revealed a negative test for salicylates. The child's general condition was quite satisfactory.

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Respirations were still hyperpnœic, but the child was generally more comfortable and fell asleep. She was then transferred to the Ottawa General Hospital. Through the courtesy of Dr. George Campbell, pædiatrician-in-chief of that institution, the child's further progress was made available to us. Shortly after admission to the General Hospital the child's condition became worse. At 6.30 p.m., on March 4, 1940, a continuous intravenous injection of 10 per cent glucose in normal saline was started. During the course of this the child convulsed and became cyanotic. The intravenous was stopped and oxygen and epinephrine were given. However, the child died at 9.05 p.m., March 4, 1940, despite this.

No post-mortem examination was obtained.

CASE 2

This case came to the attention of one of us (W.T.S.) in his capacity as coroner. The autopsy was performed by Dr. T. R. Little.

A 32 months old female took some oil of wintergreen off a shelf in the home at 9.30 a.m., April 26, 1940. The mother heard her cough and noticed that there was some of the "liniment" on a chair and on the baby's clothes. About ½ oz. was missing from the bottle. It was estimated that about 2 teaspoonfuls were on the chair and an unknown amount on the child's clothing. The child therefore had swallowed not more than 2 teaspoonfuls (8 c.c.) of the oil.

The mother gave her milk immediately. One hour later the child began to vomit. At 11 a.m., she was put to bed and vomited again. The mother telephoned a pharmacist for advice. He suggested that the administration of milk was a perfectly satisfactory procedure. The child was not very active during the day. At 9.00 p.m. she developed hyperpnœa. At 9.30 p.m. the mother asked a physician for advice over the phone. Apparently unaware of the details, he suggested that the child be given some "Frosst's".

About 2 a.m. the child's condition was such that the mother called a physician. He gave some coramine hypodermically, following which the vomiting stopped and the respirations were not so prominent. The baby asked for a drink. Thereafter, the child's sleep was broken by continual requests for fluids.

On April 27th, at 9.30 a.m., it was noticed that the child's eyes were "looking up" and that she couldn't drink well because "it was hard to swallow". Her physician was called again and immediate admission to hospital was urged. However, before other than supportive treatment could even begin the child died at 11 a.m.

The autopsy was done 6 hours later and essentially showed the following.

Considerable hyperæmia of the dependent parts and of the head and neck. The pupils were pin-point. The mucous membrane of the mouth was very dry and pale. The lips were cyanotic. The abdomen was moderately distended.

Fluid blood was in the heart. A CO_2 combining power on the heart's blood was 42 volumes per cent. The liver on section showed congestion. The kidneys and ureters were normal, grossly, except for congestion. The bladder contained 150 c.c. of urine, which showed a very strongly positive test for acetone and salicylates; sugar and albumin were absent. Microscopically, the specimen was negative.

Dr. Little noted that "most of the organs were very sticky and hyperæmic". Both lungs were collapsed and intensely congested. The subpleural and subpericardial (spaces) and meninges showed large numbers of various-sized hæmorrhages. Some of the larger ones measured 15 x 10 mm. The stomach and intestinal mucosæ were only slightly congested, but had a faint odour of wintergreen. The liver and kidneys were moderately swollen and congested. The stomach contents gave a very faintly positive test for salicylate.

Sections from the liver, kidney, brain and spleen showed no obvious pathological change, other than acute congestion.

It will be observed that in both these cases the fact that oil of wintergreen is a poison was unknown to the parents, and hence considerable delay occurred before medical treatment was instituted. Conversation with members of the profession itself reveals that the deadliness and insidiousness of this poison is not appreciated by many well-trained colleagues, although it is realized that methyl salicylate has poisonous properties. The literature on this substance repeatedly suggests that it be labelled as a poison.

That these suggestions are most legitimately put forward is demonstrated in Stevenson's[7] paper on the subject. He collected 46 cases of victims of this accident, of which 41 per cent occurred in children under circumstances similar to ours. The total mortality for the series was 59 per cent. In four cases the drug was taken with suicidal intent. The others were cases in which the ingestion was accidental.

To the total collected by Stevenson may be added one case each reported by Bowen *et al.*,[2] Dodd *et al.*,[3] Eimas,[4] and two by Baxter *et al.*[1] A further case attributed to cutaneous administration of the oil is reported by Lawson and Kaiser.[10] With the two cases described in this paper the number of reported cases of poisoning by ingestion of methyl salicylate totals 53, of which 32 were fatal, a mortality of 60.4 per cent. It would appear, then, that a review of certain features of oil of wintergreen poisoning would not be amiss.

DISCUSSION

The pathological findings in our Case 2 are similar to those found in other autopsy reports on this subject. Nothing specifically characteristic was noted, although the subpleural, subpericardial, and meningeal hæmorrhages in our case seemed to be more prominent than in the other autopsies. On the other hand, the usual findings of cloudy swelling of the heart, liver and kidneys had apparently not yet occurred. Congestion of the organs, however, was prominent. The feature of fluid blood, emphasized by Woodbury and Nicholls,[8] was present here also. It is important to note that salicylate was found in the stomach as long as 25½ hours after ingestion and despite considerable vomiting. We would like to point out that the kidney findings

in our case, as well as in many of the other reported autopsies, did not show overwhelming pathological changes.

The clinical features of our cases are in line with those commonly found. Vomiting is an early occurrence. Thereafter, rapid respirations ensue, a common time for their appearance being about 6 hours after ingestion.[7] This time-interval elapsed in Case 1, but it was longer in manifesting itself in Case 2. The respirations may be as rapid as 64 per minute.[1] They may be very deep and indeed may simulate the Kussmaul type of breathing, although most observers agree that they are more rapid than would be expected when compared with the CO_2 combining power of the blood.

Thirst is another symptom which is commonly seen. This was manifested in both our cases. Convulsions, stupor, drowsiness and coma have been noted. Cyanosis, flushed skin, tinnitus and dimness of vision are also mentioned. As a rule the temperature is only slightly elevated. The pulse may or may not be increased. For the practitioner who is called to see the case originally it must be emphasized that at first the patient does not present an alarming appearance. It is only later on in the course of the poisoning that he looks acutely ill. Fatalities have been reported following the ingestion of as little as 4 c.c.[4, 6] In our Case 2 an amount not exceeding 8 c.c. ended disastrously.

Laboratory examinations show that the urine gives a positive ferric chloride test to salicylates. Acetonuria was present in all except one case. Benedict's solution is frequently reduced. This is usually a false positive sugar reaction. Albumin may be present but not in great amount. Casts and red blood cells have also been noted.

The chemical changes in the blood are of particular interest. They reveal evidence of impaired renal function. There is increased non-protein nitrogen, chlorides and phosphates. Blood sugar may be elevated. A blood pH of 7.33 is recorded in one case,[6] but this reading was obtained only after treatment and was accompanied by a rise in CO_2 combining power from the original of 14.7 volumes per cent to 51 volumes per cent.

Total base is decreased, and CO_2 combining power is reduced generally, although there have been cases where there has been no reduction in the latter, or only slight reduction. The lowest recorded reading was 14.7 volumes per cent. The average, as calculated by Stevenson, was 32.7 volumes per cent.

The hyperpnœa, low blood CO_2, acetonuria, and the reduction of Benedict's solution have led to the diagnosis of diabetic acidosis being made in error. The similarity to diabetic acidosis has apparently resulted in the condition being treated along the lines of an out and out acidotic state. However, the recent experimental work on salicylate poisoning by Dodd, Minot and Arena[3] confirms the findings of earlier workers[11] that the acidosis is really a late occurrence and in reality may be regarded as a complicating feature.

As was previously pointed out, hyperpnœa is a common clinical finding in oil of wintergreen poisoning. The respirations are frequently more rapid than the blood CO_2 combining power would imply, if the lowered value of the latter is taken as an indication of acidosis. Odin has demonstrated an elevated pH in the blood and urine. Later on in the course of the poisoning however, the urine was found to be more acid. In experiments on dogs who were given various salicylates in varying dosages, Dodd, Minot and Arena found the blood pH to be slightly elevated and the urine to be alkaline in association with the initial hyperpnœa. This can be explained on the basis of the occurrence of a hyperventilation alkalosis, *i.e.*, the hyperpnœa blows off CO_2 and, as a compensatory feature, alkali is excreted by the kidney in an attempt to maintain the normal ratio of $\frac{H_2CO_3}{BHCO_3} = 1/20$. The hyperventilation also can explain the low total base in the blood referred to previously.

Dodd, Minot and Arena also found that the metabolic rates of their dogs were increased. This confirmed the observations of Barbour, and was further substantiated by a demonstration of the phenomenon on one of their own investigators. They found too, that when the dissipation of heat through the tongues of the dogs was interfered with by the insertion of an intratracheal cannula hyperpyrexia resulted. With the hyperpyrexia the respiratory rate increased. Dissipation of heat was then aided artificially before salicylate administration by cooling the animals by means of alcohol applications and an electric fan. Both the hyperpyrexia and the hyperpnœa could be prevented even though metabolism had increased 300 to 400 per cent of the normal. Once the hyperpyrexia was established, however, it was much more difficult to

improve the animal's condition by cooling. They concluded that the sensation of heat was an important factor in producing the hyperpnœa. Odin,[11] on the other hand, felt the hyperpnœa to be due to central stimulation.

Whether or not one can apply the findings on dogs to human physiology in this case, it would nevertheless appear that the hyperpnœa is essentially due to an effect *per se* of salicylate ingestion and primarily is not due to acidosis. In other words, the rapid breathing may *produce* chemical changes in the blood, but, in the case of salicylate poisoning, is not the ***result*** of the changes. Later on in these cases a real acidosis is present. This is explained on the basis of loss of water, combined with increased metabolism, which latter is due partly to the effect of the drug and partly to the increased temperature. This last factor cannot be a particularly important one in human beings since most of the temperatures recorded by Stevenson are not high. The increased metabolism due to the drug itself and loss of water occurs in human beings. Fluid is lost in the vomitus and by means of the diaphoretic effects of the drug. Diuresis is also a factor.[5] It has been suggested[3] that fluid intake is also diminished by the lack of co-operation of the patient. Rapid breathing also would be expected to increase the loss of fluid via the respiratory tract.

There is present, then, an increased requirement for fluid due to metabolic changes, an increased excretion of fluid and a diminished intake. All three of these factors contribute to a dehydration, as a result of which the kidney is unable to function properly and acid metabolites accumulate in the blood stream to produce an acidosis. Coupled with this, the diminished food intake plus the high metabolic rate soon consumes the food reserves of the body and ketosis develops. Further, electrolytes are lost early through the kidney, skin and gastro-intestinal tract (vomiting). All these contribute to making the conservation of a normal acid-base metabolism still more difficult and the patient may then succumb from dehydration and acidosis. Meanwhile, the element of exhaustion as a result, in part, of the persistently rapid respirations may contribute further damage to the organism, so much so that heart-failure may ensue.

It would appear then, that the problem of prime importance in treatment is to supply adequate fluids. Since the kidney usually functions well at first, this may be given as hypotonic saline with added dextrose. If this is not retained by mouth it may be given parenterally. Such a solution will provide water to help rid the body of salicylates and retained metabolic products, all of which require extra water for their excretion. It will allow for the increased loss of water from the respiratory tract. It also will provide electrolytes which can be selectively utilized by the kidney to correct depleted reserves and it will supply an antiketogenic substance to rid the body of the ketone acids.

In the more severe cases where an acidosis has supervened alkali therapy may prove of greater service. This may be given as sodium bicarbonate or sodium lactate. The latter apparently has produced no startling results in the few cases reported in which it was used. One of us (L.N.P.) during his post-graduate studies, had occasion to see another fatal case in which sodium lactate was used but in which there was no appreciable effect on the CO_2 combining power of the blood. In the early stages then, when an alkalosis exists due to hyperventilation, it would seem that alkali is contraindicated.

The water required by the body for evaporation to keep down the temperature due to increased metabolism may be in part conserved by giving alcohol sponges as frequently as possible, particularly in the presence of a tendency for the temperature to rise. This would also aid in diminishing any increase in respiratory rate due to the sensation of heat. The early rapid respirations may be controlled by giving morphine, which would also guard the patient to some degree against exhaustion, by giving him rest and favourably influence water balance.

In view of the presence of oil of wintergreen in the stomach even after twenty-four hours, gastric lavage is indicated in every case to aid in the washing out of any residual poison. For the same reason, since there is sometimes the odour of wintergreen in the stools, colonic lavage would also seem to be advisable. In cyanosis oxygen is of course indicated and in the presence of beginning heart failure, rapid digitalization would be advisable.

In any event it is of the utmost importance to watch the subject of the poisoning very carefully and above all not to be lulled into a false sense of security by the satisfactory appearance of a patient suffering from this condi-

tion. As a necessary precautionary measure one should not be content with a mere washing out of the stomach. The routine outlined above is a simple one and is worth being used even though one may feel that the oil of wintergreen has been vomited or washed out of the gastro-intestinal tract. Only small residual amounts are required for fatality to occur.

Further, as illustrated by our Case 1, the fact that no more salicylate was being excreted in the urine does not mean that the patient is out of danger. Stevenson quotes figures which indicate that only 51 per cent of methyl salicylate as "salicyl radicle is recoverable from the urine and its excretion is completed in four days".

In our first case it is possible that the child's improvement following the giving of large amounts of fluid was sufficient to make us feel that the child was out of danger and could be moved. Apparently, this was not the case. Unfortunately, not only were the blood studies incomplete but a post-mortem could not be obtained. A suitable explanation for the death, other than the general one of poisoning due to methyl salicylate, cannot be offered.

SUMMARY

1. Seven cases of poisoning following the ingestion of methyl salicylate, and one following its cutaneous administration are added to the list compiled by Stevenson.

2. The high mortality is emphasized.

3. A plea for the proper labelling of the substance as a poison is reiterated.

4. A warning against optimism induced by the appearance of the patient is made.

5. A discussion on the chemical changes is presented.

6. A suggested treatment is outlined based on these changes. It is essentially that recommended by Dodd, Minot and Arena.

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Case Reports

PNEUMOCOCCAL PERITONITIS TREATED BY SULFAPYRIDINE

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Recently a case of pneumococcal peritonitis appeared on our service. This condition always carries with it a grave prognosis, which is variously quoted as having a mortality of 40 to 60 per cent, regardless of the type of therapy used, be it medical, surgical or a combination of both. This case is interesting in that the patient recovered after an uneventful convalescence, following the use of surgery and sulfapyridine.

The patient (M.D.B.) was a girl of five years of age who had been perfectly well until about ten days prior to admission, at which time she contracted a sore throat. She recovered from this in a few days. Then on the day prior to admission, she began to have lower abdominal pain, associated with fever, vomiting, and lower abdominal tenderness. She passed a greenish stool but there was no diarrhœa or constipation. The pain grew more severe during the night and the other symptoms showed no remission.

Physical examination revealed an acutely ill child with a temperature of 104.6°; pulse, 144; respiration, 30; white blood count 33,400; the urine showed a faint trace of albumin. The patient had a Hippocratic facies with flushed cheeks. The tongue was moist. Distension was not marked, but there was generalized lower abdominal tenderness and moderate muscle spasm. No dullness on percussion. Occasional peristaltic sounds could be heard. Throat and heart were negative. There was a suggestion of a few moist râles in the right base of the chest.

A diagnosis of acute suppurative appendicitis with perforation or pneumococcal peritonitis was made. Laparotomy was performed. On opening the peritoneal cavity sticky odourless purulent fluid presented. Cultures and smears were taken for bacteriological examination. The appendix was isolated and found to be acutely inflamed. It was removed. The regional lymph glands were markedly enlarged. No Meckel's diverticulum or other pathological condition was found. The wound was closed with drainage. The smear taken at operation was reported as showing pneumococci, which was confirmed the following day by culture of a pure growth of this organism.

During this period the child had delirium, a temperature 105.4°, and a pulse of 160, despite interstitial saline and proctoclysis. Abdominal distension was treated with linseed poultices, and restlessness with Tinct. Camph. Co., minims xv, q. 4 h. As soon as the cultures were reported, sulfapyridine was administered in doses of grains vii ss q. 6 h. The temperature at that time was 105°, the pulse 136, respirations 44. In twenty-four hours the tempera-